induced immune dysfunctions selected from the group consisting of including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human animal interaction stress in dogs.

37. A pharmaceutical composition as claimed in claim 14 for treatment of fibromyalgia.

38. A pharmaceutical composition as claimed in claim 14 for treatment of anorexia or bulimia nervosa.

39. A pharmaceutical composition as claimed in claim 14 for treatment of cerebral ischemia, selected from the group consisting of cerebral hippocampal ischemia; excitotoxic neuronal damage.

40. A pharmaceutical composition as claimed in claim 14 for treatment of including social phobia, agoraphobia or specific phobias

REMARKS

A copy of claims 1, 2,, 3, 4, 13 and 14, showing the amendments thereto is attached as an Appendix.

A new paragraph has been inserted on page 1 to set out the applications from which benefit is claimed. This application was filed prior to November 29, 2000 so that no petition is required. In any case priority claims were made on the declaration filed on this application.

On the issue raised in paragraph 7 of the action, it is pointed out that Application Serial No 09/254387 is a U.S. national stage entry of International Patent Application PCT/IB95/00437 which was filed on June 6, 1995. Since 35 USC 363 provides that such International Application has, with one exception, "the effect of a national patent application" it is submitted that the declaration properly set out the date of June 6, 1995 as the filing date of Serial No 09/254387 and that no new declaration ids required.

The rejections under 35 USC 112 have been met. In most cases, the corrections made are self-evident. References to Z groups and Formulae I and III have been deleted as being irrelevant to what is now claimed. So far as the use of the terms"alkyl", alkylene", "cycloalkyl" and "cycloalkylene" including unsaturation is concerned, page 36 lines 3 to 5 make it clear that the use of these terms in the present application was in some cases intended to include unsaturated

groups. In an effort to meet the examiner's concerns, where appropriate, the term "hydrocarbyl" and its derivatives has been used to replace the terms questioned by the Examiner in those definitions where the original text makes it clear that the group in question is one where reference is made to the presence of possible double or triple bonds, namely the R_1 (alkyl, alkylene, cycloalkyl, cycloalkylene and heterocycloalkyl), R_2 (alkyl, alkylene, cycloalkyl, cycloalkylene and heterocycloalkyl), R_4 (alkyl and alkylene) R_5 alkyl and alkylene). New claim 29 is based on language that was included in claim 1 as filed as being "especial" possibilities as R_{24} and R_{25}.

The rejection under 35 USC 102 is respectfully traversed. As noted above, the present application claims the benefit of Application Serial No 09/254387 which has a filing date of June 6, 1995. This date is prior to the publication date of WO 95/33750. Furthermore, even if this were not the case, it is pointed out that the present applicant is the same person as the author of WO/9533750 so that it is simply not possible for this document to disclose the same invention as now claimed on a date prior to the present applicant's having made such invention.

In view of the foregoing it is believed that this application is now in order for allowance. An early action to this end is respectfully solicited. If the Examiner believes it would be useful to discuss this matter either personally or in a telephone interview, he is requested to let us know so that this can be arranged.

Respectfully submitted,

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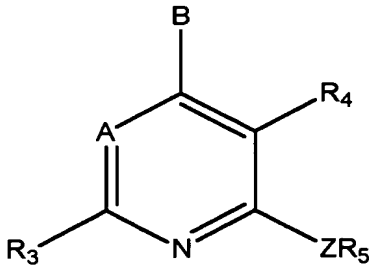
Appendix

1(Amended) A compound of the formula



I

or a pharmaceutically acceptable salt thereof, wherein

A is CR_7;

B is $-NR_1R_2$, $-CR_1R_2R_{11}$, $-C(=CR_2R_{12})R_1$, $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_2OR_1$, $-CHR_1OR_2$, $-CHR_2SR_1$,$-C(S)R_2$, $-C(O)R_2$, $-CHR_2NR_1R2$, $-CHR_1NHR_2$, $-CHR_1N(CH_3)R_2$, or $-NR_{12}NR_1R_2$;

Yis CH or N;

Z is NH, O, S, ~~$-N(C_1$-C_2 alkyl), $-NC(O)CF_3$, or $-C(R_{13}R_{14})$~~, $-N(C_1$-C_2 alkyl)-, $-NC(O)CF_3$,- or $-C(R_{13}R_{14})$- wherein R_{13} and R_{14} are each, independently, hydrogen, trifluoromethyl or methyl, or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl, or $-C(R_{13}R_{14})$ is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R_5, which ring optionally comprises two or three further hetero members selected independently from oxygen, nitrogen, NR_{12}, and $S(O)_m$, and optionally comprises from one to three double bonds, and is optionally substituted with halo, C_1- C_4 alkyl, $-O(C_1$-C_4 alkyl), NH_2, $NHCH_3$, $N(CH_3)_2$, CF_3, or OCF_3, with the proviso that said ring does not contain any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and does not comprise more than two oxygen or $S(O)_m$ heterologous members;

R_1 is C(O)H, $C(O)(C_1$-C_6 ~~alkyl~~ hydrocarbyl), $C(O)(C_1$-C_6 ~~alkylene~~ hydrocarbylene)(C_3-C_8 ~~cycloalkyl~~ cyclohydrocarbyl), $C(O)(C_3$-C_8 ~~cycloalkylene~~ cyclohydrocarbylene)(C_3-C_8 ~~cycloalkyl~~ cyclohydrocarbyl), $C(O)(C_1$-C_6 ~~alkylene~~ hydrocarbylene)(C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl), $-C(O)(C_3$-C_8 ~~cycloalkylene~~ cyclohydrocarbylene)(C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl), C_1-C_6 ~~alkyl~~ hydrocarbyl, C_3-C_8 ~~cycloalkyl~~ cyclohydrocarbyl , C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl, $-(C_1$-C_6 ~~alkylene~~ hydrocarbylene (C_3-C_8 ~~cycloalkyl~~ cyclohydrocarbyl),C_3-C_8 ~~cycloalkylene~~ cyclohydrocarbylene)(C_3-C_8 ~~cycloalkyl~~ cyclohydrocarbyl), $-(C_1$-C_6 ~~alkylene~~ hydrocarbylene)(C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl), $-(C_3$-C_8 ~~cycloalkylene~~

cyclohydrocarbylene)(C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl), or -O-aryl, or -O-(C_1-C_6 ~~alkylene~~ hydrocarbylene)-aryl; wherein said aryl, C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl, C_1-C_6 ~~alkyl~~ hydrocarbyl, C_3-C_8 ~~cycloalkyl~~ cyclohydrocarbyl , C_3-C_8 ~~cycloalkylene~~ cyclohydrocarbylene, and C_1-C_6 ~~alkylene~~ hydrocarbylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents R_8 independently selected from the group consisting of C_1-C_4 ~~alkyl~~ hydrocarbyl, -C_3-C_8 ~~cycloalkyl~~ cyclohydrocarbyl , hydroxy, chloro, bromo, iodo, CF_3, -O-(C_1-C_6 ~~alkyl~~ hydrocarbyl), -O-(C_3-C_5 ~~cycloalkyl~~ cyclohydrocarbyl), -O-CO-(C_1-C_4 ~~alkyl~~ hydrocarbyl), -O-CO-NH(C_1-C_4 ~~alkyl~~ hydrocarbyl), -O-CO-N(R_{24})(R_{25}), -N(R_{24})(R_{25}), -S(C_1-C_4 ~~alkyl~~ hydrocarbyl), -S(C_3-C_5 ~~cycloalkyl~~) cyclohydrocarbyl --N(C_1-C_4~~alkyl~~ hydrocarbyl)CO(C_1-C_4 ~~alkyl~~ hydrocarbyl), -NHCO(C_1-C_4 ~~alkyl~~ hydrocarbyl), -COO(C_1-C_4 ~~alkyl~~ hydrocarbyl), -CONH(C_1-C_4 ~~alkyl~~ hydrocarbyl), -CONC$_1$-C_4 ~~alkyl~~ hydrocarbyl)(C_1-C_2 ~~alkyl~~ hydrocarbyl), CN, NO_2, -OSO_2(C_1-C_4 ~~alkyl~~ hydrocarbyl), S^+(C_1-C_6 ~~alkyl~~ hydrocarbyl)(C_1-C_2 ~~alkyl~~ hydrocarbyl), -SO(C_1-C_4 ~~alkyl~~ hydrocarbyl) and -SO_2(C_1-C_4 ~~alkyl~~ hydrocarbyl); and wherein the C_1-C_6 ~~alkyl~~ hydrocarbyl, C_1-C_6 ~~alkylene~~ hydrocarbylene, C_5-C_8 ~~cycloalkyl~~ cyclohydrocarbyl, C_5-C_8 ~~cycloalkylene~~ cyclohydrocarbylene, and C_5-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl moieties of R_1 may optionally independently contain from one to three double or triple bonds; and wherein the C_1-C_4 ~~alkyl~~ hydrocarbyl moieties and C_1-C_6 ~~alkyl~~ hydrocarbyl moieties of R_8 can optionally independently be substituted with hydroxy, amino, C_1-C_4 alkyl, aryl, -CH_2-aryl$_1$ C_3-C_5 cycloalkyl, or -O-(C_1-C_4 alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally contain one or two double or triple bonds; and wherein each ~~heterocycloalkyl~~ heterocyclohydrocarbyl group of R_1 contains from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12};

R_2 is hydrogen, C_1-C_{12} ~~alkyl~~ hydrocarbyl, C_3-C_8 ~~cycloalkyl~~ cyclohydrocarbyl , C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl, -(C_1-C_6 ~~alkylene~~ hydrocarbylene)(C_3-C_8 ~~cycloalkyl~~ cyclohydrocarbyl), -(C_3-C_8 ~~cycloalkylene~~ cyclohydrocarbylene)(C_3-C_8 ~~cycloalkyl~~ cyclohydrocarbyl), -(C_1-C_6 ~~alkylene~~ hydrocarbylene)(C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl), -(C_3-C_6 ~~cycloalkylene~~ cyclohydrocarbylene)(C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl), aryl, -(C_1-C_6 ~~alkylene~~ hydrocarbylene)aryl, or -(C_3-C_8 ~~cycloalkylene~~ cyclohydrocarbylene)(aryl); wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C_1-C_6 alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C_1-C_6 alkoxy, -OH, -O-CO-(C_1-C_6 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -S (C_1-C_6 alkyl), -S(O)(C_1-C_6 alkyl), -$S(O)_2$(C_1-C_6 alkyl), S^+(C_1-C_6 alkyl)(C_1-C_2 alkyl)I', CN, and NO_2; and

wherein the C_1-C_{12} ~~alkyl~~ hydrocarbyl, -(C_1-C_6 ~~alkylene~~ hydrocarbylene), ~~-(C_5-C_8-cycloalkyl), -(C_5-C_8-cycloalkylene), and -(C_5-C_8-heterocycloalkyl)~~ and cyclohydrocarbyl gropups of 5 - 8 carbon atoms, cyclohydrocarbylene groups of 5 to 8 carbon atoms and heterocyclohydrocarbyl groiups of 5 to 8 atoms ~~moieties~~ of R_2 may optionally independently contain from one to three double or triple bonds; and wherein each ~~heterocycloalkyl~~ heterocyclohydrocarbyl group of R_2 contains from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12};

or when R_1 and R_2 are as in -$NHCHR_1R_2$, -$OCHR_1R_2$, -$SCHR_1R_2$, -CHR_1R_2 or -NR_1R_2, R_1 and R_2 of B may form a saturated 5- to 8-membered ring which may optionally contain one or two double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen, $S(O)_m$, nitrogen or NR_{12}; and which carbocyclic ring can optionally be substituted with from 1 to 3 substituents selected from the group consisting of hydroxy, C_1-C_4 alkyl, fluoro, chloro, bromo, iodo, CF_3, -O-(C_1-C_4 alkyl), -O-CO-(C_1-C_4 alkyl), -O-CO-NH(C_1-C_4 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -NH(C_1-C_4 alkyl), -N(C_1-C_2 alkyl)(C_1-C_4 alkyl), -S(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)CO(C_1-C_4 alkyl), -NHCO(C_1-C_4 alkyl),-COO(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -CON(C_1-C_4 alkyl)(C_1-C_2 alkyl), CN, NO_2, -OSO_2(C_1-C_4 alkyl), -SO(C_1-C_4 alkyl), and -SO(C_1-C_4 alkyl), wherein one of said one to three substituents can further be selected from phenyl;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3, NH_2, NH(C_1-C_2 alkyl), $N(CH_3)_2$, -$NHCOCF_3$, -$NHCH_2CF_3$, $S(O)_m$(C_1-C_4 alkyl), $CONH_2$, -$CONHCH_3$, $CON(CH_3)_2$, -CF_3, or CH_2OCH_3;

R_4 is hydrogen, C_1-C_4 ~~alkyl~~ hydrocarbyl, C_3-C_5 cycloalkyl, -(C_1-C_4 ~~alkylene~~ hydrocarbylene)(C_3-C_5 cycloalkyl), -(C_3-C_5 cycloalkylene)(C3-C6 cycloalkyl), cyano, fluoro, chloro, bromo, iodo, -OR_{24} C_1-C_6 alkoxy, -O- cycloalkyl), -O-(C_1-C_4 ~~alkylene~~ hydrocarbylene)(C_3-C_5 cycloalkyl), -O-(C_3-C_5 cycloalkylene)(C_3-C_5 cycloalkyl), -$CH_2SC(S)O$(C_1-C_4 alkyl), ~~-CH_2OF_3~~ CH_2OCF_3, CF_3, amino, nitro, -$NR_{24}R_{25}$, -(C_1-C_4 ~~alkylene~~ hydrocarbylene)-OR_{24}, -(C_1-C_4 ~~alkylene~~ hydrocarbylene)Cl, -(C_1-C_4 ~~alkylene~~ hydrocarbylene)$NR_{24}R_{25}$, -$NHCOR_{24}$, -$NHCONR_{24}R_{25}$, ~~-C=NOR$_{24}$~~ -CH=NOR_{24}, -$NHNR_{24}R_{25}$, -$S(O)_mR_{24}$, -$C(O)R_{24}$, -$OC(O)R_{24}$, -C(O)CN, -$C(O)NR_{24}R_{25}$, -$C(O)NHNR_{24}R_{25}$, and -$COOR_{24}$, wherein the ~~alkyl~~ hydrocarbyl and ~~alkylene~~ hydrocarbylene groups of R_4 may optionally independently contain one or two double or triple bonds and may optionally independently be substituted with one or two substituents R_{10} independently selected from hydroxy, amino, -$NHCOCH_3$, -$NHCOCH_2Cl$, -NH(C_1-C_2 alkyl), -N(C_1-C_2 alkyl)(C_1-C_2alkyl), -COO(C_1-C_4 alkyl), -COOH, -CO(C_1-C_4 alkyl), C_1-C_6 alkoxy, C_1-C_3 thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R_5 is aryl or heteroaryl and is substituted with from one to four substituents R_{27}

independently selected from halo, C_1-C_{10} ~~alkyl~~ hydrocarbyl, -(C_1-C_4 ~~alkylene~~ hydrocarbylene)(C_3-C_8 cycloalkyl), -(C_1-C_4 ~~alkylene~~ hydrocarbylene)(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkyl), -(C_4-C_8 heterocycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_4-C_8 heterocycloalkyl), C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, nitro, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $-NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, ~~$-CO(NOR_{22})R_{23}$~~ $-CON(OR_{22})R_{23}$, $-CO_2R_{26}$, $-C{=}N(OR_{22})R_{23}$, and $-S(O)_mR_{23}$; wherein said C_1-C_{10} alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 ~~alkylene~~ hydrocarbylene), (C_3-C_8 cycloalkyl), (C_3-C_8 cycloalkylene), and (C_4-C_8 heterocycloalkyl) groups can be optionally substituted with from one to three substituents independently selected form C_1-C_4 alkyl, C_3-C_8 cycloalkyl, (C_1-C_4 ~~alkylene~~ hydrocarbylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), C_1-C_4 haloalkyl, hydroxy, C_1-C_6 alkoxy, nitro, halo, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26}, $-CO(NOR_{22})R_{25}$, and $-S(O)_mR_{23}$; and wherein two adjacent substituents of the R_5 group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to ~~R^5~~ R_5, which ring optionally can contain one, two, or three heterologous members independently selected from O, $S(O)_m$, and N, but not any -S-S-, -O-O-, -S-O-, or -N-S- bonds, and which ring is optionally substituted with C_1-C_4 alkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cyloalkylene)(C_3-C_8 cycloalkyl), C_1-C_4 haloalkyl, nitro, halo, cyano $-NR_{24}R_{25}$, $NR_{24}COR_{25}$, $NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, CO_2R_{26}, $-CO(NOR_{26})R_{25}$, or $-S(O)_mR_{23}$; wherein one of said one to four optional substituents R_{27}, can further be selected from $-SO_2NH(C_1$-C_4 alkyl), $-SO_2NH(C_1$-C_4 alkylene)(C_3-C_8 cycloalkyl), $SO_2NH(C_3$-C_8 cycloalkyl), $-SO_2NH(C_3$-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), $-SO_2N(C_1$-C_4 alkyl)(C_1-C_2 alkyl), $-SO_2NH_2$, $-NHSO_2(C_1$-C_4 alkyl), $-NHSO_2(C_3$-C_8 cycloalkyl), $-NHSO_2(C_1$-C_4 alkylene)(C_3-C_8 cycloalkyl), and $-NHSO_2(C_3$-C_8 cycloalkylene)(C_3-C_8 cycloalkyl); and wherein the ~~alkyl~~ hydrocarbyl, and ~~alkylene~~ hydrocarbylene groups of R_5 may independently optionally contain one double or triple bond;

R_7 is hydrogen, methyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, -O(C_1 - C_2)alkyl), -O(cyclopropyl), - COO(C_1- C_2 alkyl), -COO(C_3-C_8 cycloalkyl), $-OCF_3$, $-CF_3$, $-CH_2OH$ or CH_2OCH_3;

R_{11} is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R_{12} is hydrogen or C_1-C_4 alkyl;

R_{22} is independently at each occurrence selected from hydrogen, C_1-C_4 alkyl, C,-C4 haloalkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_8 cycloalkyl, (C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), and (C_1-C_4 alkylene)(C_3-C_8 cycloalkyl);

R_{22} is independently at each occurrence selected from hydrogen, C_1-C_{14} alkyl, C_1-C_{14} haloalkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, C_3-C_8 cycloalkyl, (C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), and (C_1-C_4) alkylene)(C_3-C_8 cycloalkyl);

R_{23} is independently at each occurrence selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_2-C_8 alkoxyalkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), aryl, -(C_1-C_4 alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

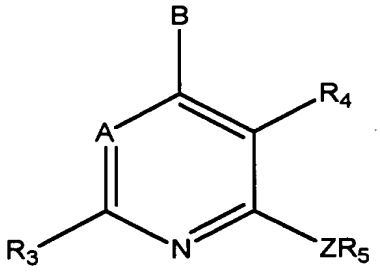
R_{24} and R_{25} are independently at each occurrence selected from hydrogen, -C_1-C_4 alkyl, C_1-C_4 haloalkyl, ~~especially CF_3, CHF_2, CF_2CF_3, or CH_2CF_3,~~ -(C_1-C_4 alkylene)OH, -(C_1-C_4 alkylene)-O-(C_1-C_4 alkyl), -(C_1-C_4 alkylene)-O-(C_3-C_5 cycloalkyl), C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), -C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl , -(C_1-C_4 alkylene)(C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyll), -(C_3-C_8 cycloalkylene)(C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl), aryl, and -(C_1-C_4 alkylene)(aryl), wherein the -C_4-C_8 ~~heterocycloalkyl~~ heterocyclohydrocarbyl groups can each independently optionally be substituted with aryl, CH_2-aryl, or C_1-C_4 alkyl, and can optionally contain one or two double or triple bonds; or, when R_{24} and R_{25} are as $NR_{24}R_{25}$, -$C(O)NR_{24}R_{25}$, -(C_1-C_4 alkylene)$NR_{24}R_{25}$, or -$NHCONR_{24}R_{25}$, then $NR_{24}R_{25}$ may further optionally form a 4 to 8 membered heterocyclic ring optionally containing one or two further hetero members independently selected from $S(O)_m$, oxygen, nitrogen, and NR_{12}, and optionally containing from one to three double bonds;

R_{26} is independently at each occurrence selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_8 cycloalkyl, -(C_1-C_4 alkylene)(C_3-C_8 cycloalkyl), -(C_3-C_8 cycloalkylene)(C_3-C_8 cycloalkyl), aryl, and -(C_1-C_4 alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that ~~heterocycloalkyl~~ heterocyclohydrocarbylene groups of the compound of formula I, ~~II~~, ~~or III~~ do not comprise any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and do not comprise more than two oxygen or $S(O)_m$ heterologous members.

2. A compound according to claim 1 of the formula



or a pharmaceutically acceptable salt thereof, wherein

A isCR_7;

B is $-NR_1R_2$, $-CR_1R_2R_{11}$, $-C(=CR_2R_{12})R_1$, $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_2OR_{12}$, $-CHR_2SR_{12}$, $-C(S)R_2$ or $-C(O)R_2$;

Z is -NH, O, S, N(C_1-C_2 alkyl) or C($R_{13}R_{14}$) wherein R_{13} and R_{14} are each independently, hydrogen, trifluoromethyl or methyl or one of R_{13} and R_{14} is cyano and the other is hydrogen or methyl;

R_1 is C_1-C_6 ~~alkyl~~ hydrocarbyl which may optionally be substituted with one or two substituents R_8 independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, CF_3, C $_1$-C_4 alkoxy, -O-CO-(C_1-C_4 a ~~alkyl~~ hydrocarbyl), -O-CO-NH(C_1-C_4 ~~alkyl~~ hydrocarbyl), -O-CO-N(C_1-C_4 ~~alkyl~~ hydrocarbyl)(C_1-C_2 ~~alkyl~~ hydrocarbyl), -NH(C_1-C_4 ~~alkyl~~ hydrocarbyl), -N(C_1-C_2 alkyl)(C_1-C_4 ~~alkyl~~ hydrocarbyl), -S(C_1-C_4 alkyl), -N(C_1-C_4)CO(C_1-C_4 ~~alkyl~~ hydrocarbyl), -NHCO(C_1-C_4 ~~alkyl~~ hydrocarbyl), -COO(C_1-C_4 ~~alkyl~~ hydrocarbyl)~~alkyl~~ hydrocarbyl, -CONH(C_1-C_4 ~~alkyl~~ hydrocarbyl), -CON(C_1-C_4 ~~alkyl~~ hydrocarbyl)(C_1-C_2 alkyl), CN, NO_2, -SO(C_1-C_4 ~~alkyl~~ hydrocarbyl) and -SO_2(C_1-C_4 ~~alkyl~~ hydrocarbyl), and wherein said C_1-C_6 ~~alkyl~~ hydrocarbyl and the (C_1-C_4)~~alkyl~~ hydrocarbyl moieties in the foregoing R_1 groups may optionally contain one carbon-carbon double or triple bond;

R_2 is C_1-C_{12} ~~alkyl~~ hydrocarbyl, aryl or -(C_1-C_4 ~~alkylene~~ hydrocarbylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or -(C_1-C_6 alkylene)cycloalkyl, wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said -(C_1-C_6 alkylene)cycloalkyl having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by N-R_9 wherein R_9 is hydrogen or C_1-C_4 alkyl; and wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro and C_1-C_4 alkyl, or with one substitutent selected from bromo, iodo, C_1-C_6 alkoxy, -O-CO-(C_1-C_6 alkyl), -O-CO-N(C_1-C_4 alkyl)(C_1-C_2 alkyl), -S(C_1-C_6 alkyl), CN, NO_2, -SO(C_1-C_4 alkyl), and -SO_2(C_1-C_4 alkyl), and wherein said C_1-C_{12} ~~alkyl~~ hydrocarbyland the C_1-C_4 ~~alkylene~~ hydrocarboylene moiety of said -(C_1-C_4 ~~alkylene~~ hydrocarbylene)aryl may optionally contain one carbon-carbon double or triple bond;

or $-NR_1R_2$ or $-CR_1R_2R_{11}$ may form a saturated 5- to 8-membered carbocyclic ring which may optionally contain one or two carbon-carbon double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen or sulfur atom;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3, methylthio, methylsulfonyl, CH_2OH, or CH_2OCH_3;

R_4 is hydrogen, C_1-C_4 ~~alkyl~~ hydrocarbyl, fluoro, chloro, bromo, iodo, C_1-C_4 alkoxy, trifluoromethoxy, $-CH_2OCH_3$, $-CH_2OCH_2CH_3$, $-CH_2CH_2OCH_3$, $-CH_2OF_3$, CF_3, amino, nitro, $-NH(C_1$-C_4 alkyl), $-N(CH_3)_2$, $-NHCOCH_3$, $-NHCONHCH_3$, $-SO_n(C_1$-C_4 ~~alkyl~~ hydrocarbyl) wherein n is 0, 1 or 2, cyano, hydroxy, $-CO(C_1$-C_4 ~~alkyl~~ hydrocarbyl), -CHO, cyano or $-COO(C_1$-C_4 alkyl) wherein said C_1-C_4 ~~alkyl~~ hydrocarbyl may optionally contain one double or triple bond and may optionally be substituted with one substitutent selected from hydroxy, amino, $-NHCOCH_3$, $-NH(C_1$-C_2 alkyl), $-N(C_1$-C_2 alkyl)$_2$, $-COO(C_1$-C_4 alkyl), $-CO(C_1$-,C_4 alkyl), C_1-C_3 alkoxy, C_1-C_3 thioalkyl, fluoro, chloro, cyano and nitro;

R_5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each of the above groups R_5 is substituted with from one to three substituents independently selected from fluoro, chloro, C_1-C_6 alkyl, and C_1-C_6 alkoxy, or with one substitutent selected from hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, $-(C_1$-C_6 alkyl)$O(C_1$-$C_6)$alkyl, $-NHCH_3$, $-N(CH_3)_2$, -COOH, $-COO(C_1$-C_4 alkyl), $-CO(C_1$-C_4 alkyl), $-SO_2NH(C_1$-C_4 alkyl), $-SO_2N(C_1$-C_4 alkyl)$(C_1$-C_2 alkyl), $-SO_2NH_2$, $-NHSO_2(C_1$-C_4 alkyl), $-S(C_1$-C_6 alkyl) and $-_{SO2}(C_1$-C_6 alkyl), and wherein the C_1-C_4 alkyl and C_1-C_6 alkyl moieties of the foregoing R_5 groups may optionally be substituted with one or two fluoro groups or with one substitutent selected from hydroxy, amino, methylamino, dimethylamino and acetyl;

R_{11} is hydrogen, hydroxy, fluoro, or methoxy;

R_{12} is hydrogen or C_1-C_4 alkyl; and

or a pharmaceutically acceptable salt of such compound.

3. (Amended) A compound according to claim 2 wherein B is $-NR_1R_2$, $-NHCHR_1R_2$, $-SCHR_1R_2$ or $-OCHR_1R_2$; R_1 is C_1-C_6 ~~alkyl~~ hydrocarbyl, which may optionally be substituted with one hydroxy, fluoro, CF_3, or C_1-C_2 alkoxy group and may optionally contain one double or triple bond; and R_2 is benzyl or C_1-C_6 ~~alkyl~~ hydrocarbyl which may optionally contain one carbon-carbon double or triple bond, wherein said C_1-C_6 alkyl or the phenyl moiety of said benzyl may optionally be substituted with fluoro, CF_3, C_1-C_2 alkyl, or C_1-C_2 alkoxy.

4. (Amended) A compound according to claim 2 wherein R_1 is C_1-C_6 ~~alkyl~~ hydrocarbyl which may be substituted by fluoro, CF_3, hydroxy, C_1-C_2 alkyl or C_1-C_2 alkoxy and which may optionally contain one carbon-carbon double or triple bond.

13. (Amended) A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF, ~~including but not limited to disorders induced or facilitated by CRF~~, or (b) a disorder or condition selected from inflammatory disorders ~~such as rheumatoid arthritis and osteoarthritis~~, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception ~~such as fibromyalgia~~; mood disorders ~~such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression~~, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases ~~such as Alzheimer's disease, Parkinson's disease and Huntington's disease~~; gastrointestinal diseases; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; chemical dependencies or addictions, ~~including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs~~; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, ~~for example cerebral hippocampal ischemia; excitotoxic neuronal damage~~; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, ~~including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human animal interaction stress in dogs~~; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

14. A pharmaceutical composition according to claim 13 for the treatment of a disorder selected from inflammatory disorders ~~such as rheumatoid arthritis and osteoarthritis~~, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception ~~such as fibromyalgia~~; mood disorders such as depression, ~~including major depression, single episode depression, recurrent depression, child abuse induced depression~~, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; fatigue syndrome; stress induced headache; cancer;

irritable bowel syndrome, Crohn's disease; spastic colon; human immunodeficiency virus (HIV) infections; neurodegenerative diseases ~~such as Alzheimer's disease, Parkinson's disease and Huntington's disease~~; gastrointestinal diseases; eating disorders ~~such as anorexia and bulimia nervosa; hemorrhagic stress~~; chemical dependencies and addictions; obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions ~~including stress induced immune dysfunctions~~; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; and hypoglycemia in a mammal, including a human.